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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,716	02/26/2001	George N. Pavlakis	15280-3521US	4088

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EXAMINER	
WINKLER, ULRIKE	
ART UNIT	**PAPER NUMBER**
1648	11

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/673,716	PAVLAKIS ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE -3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's election with traverse of Group I in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the Groups all stem from the same inventive concept. This is not found persuasive because the method steps involved in using a known or described post transcription regulatory element that contains structure and function differs from a methods of finding a post transcriptional element that does not share common structure. The methods therefore utilize different protocols and materials requiring different searches in the art.

The requirement is still deemed proper and is therefore made FINAL.

Specification

Applicant is required to update the status (pending, allowed, ect.) of all parent priority applications in the first line of the specification.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The use of the term "novel" should be avoided in the title.

Sequence listing

Applicant's CRF and paper sequence listing have been entered.

Claim Objections

Claim 1-30 are objected to because of the following informalities: The claims use abbreviations such as "PRE" or "NCTE", for the sole purpose of clarity the first time the

abbreviation is used in a claim set beginning with an independent claim the full term should be used. Appropriate correction is requested.

Claim 1 additionally makes reference to (i) however there is no reference to an additional element (ii). Appropriate correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28 and 29 provides for the use of a PRE, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 28 and 29 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 21-29 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant invention is drawn to a "vaccine" for the "prophylaxis or amelioration" of a viral infection wherein the viral infection is HIV.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include: (1) the nature of the invention, (2) the state of the prior art, (3) the presence or absence of working examples, (4) the amount or direction or guidance presented,(5) the quantity of experimentation necessary, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The term "vaccine" implies any preparation intended for active immunological prophylaxis; e.g., preparations of killed microbes of virulent strains or living microbes of attenuated (variant or mutant) strains; or microbial, fungal, plant, protozoal, or metazoan derivatives or products. Although just about any protein when inoculated can cause an immune reaction, the prophylactic nature of this reaction is not guaranteed and has to be experimentally determined. Prophylaxis is defined in Stedman's Medical Dictionary as the prevention of disease or of a process that can lead to disease. This is achieved by use of an antigenic

(immunogenic) agent to actively stimulate the immunological mechanism, or the administration of chemicals or drugs to members of a community to reduce the number of carriers of a disease and to prevent others contracting the disease. Polyvalent vaccine is defined in Stedman's Medical Dictionary as comprising multiple antigens from more than one strain of a pathogenic microorganism or from a mixture of immunogens such as diphtheria, pertussis and tetanus toxoid preparations.

Vaccines stimulate the production of neutralizing antibodies, these antibodies react well with laboratory strains of HIV but react poorly with field isolates. So far research has not developed a preventative vaccine nor a therapeutic vaccine [see Fox et al. No winners against AIDS, Bio/Technology (1994) Vol. 12, pages 128]. HIV-1 and HIV-2 are similar viruses and neutralizing antibodies that recognize one virus can be cross reactive against the other virus. One of ordinary skill in the art would have an expectation that the infection with one virus which produces neutralizing antibodies would provide protection against infection with the other viral strain. This has not been observed, in dually infected persons HIV-2 does not seem to have any influence on *in vivo* HIV-1 viral load (see abstract and discussion) [see Nkengasong et al. Dual infection with human immunodeficiency virus type 1 and type 2 : impact on HIV type 1 viral load and immune activation markers in HIV-seropositve female sex workers in Abidjan, Ivory Coast. AIDS Research and Human Retroviruses (2000) Vol. 16, No. 14, pages 1371-1378] . There is some suggestion, that infection with HIV-2 might actually increase the risk of infection with HIV-1. This may be explained by the observation that antibodies against the envelope protein of HIV-2 cross react with those against HIV-1 which instead of providing protection increases the susceptibility to HIV-1. Based on the epidemiological data HIV-2 infection does

not protect against HIV-1 and is not suitable as a model for HIV-1 vaccine development [see Greenberg AE. Possible protective effect of HIV-2 against incident HIV-1 infection: review of available epidemiological and in vitro data. AIDS (2001) Vol. 15, No. 17, pages 2319-2321].

Animal models have not been informative in the development of an HIV vaccine. Chimpanzees vaccinated with several recombinant gp120 products have been protected against infection to intravenous challenge. Assays for neutralizing antibodies were preformed against laboratory adapted strains. There are significant biological differences between laboratory-adapted strains and primary isolates one being that the laboratory-adapted strain is effectively neutralized by antibodies while the primary isolate is not. Chimpanzees may be susceptible to infection by HIV they do not develop clinical disease. The limitations of this animal model, in conjunction with eh lack of natural résistance to HIV in humans means that the immune correlates of protection between animal and human remain unknown [Macola et al. Aids vaccine : are we ready for human efficacy trials ? Journal of the American Medical association (1994) Vol. 272, No. 6, pages 488-489]. Although, animal models are an essential resource for evaluating the safety and comparative immunogenicity of candidate AIDS vaccine strategies. Animal models cannot determine whether a vaccine will be effective against HIV-1 infection of humans, this can only be established in Phase II trials [Feinberg et al. Aids Vaccine Models : challenging challenge viruses. Nature Medicine (2002) Vol. 8, pages 207-210].

Due to the large quantity of experimentation necessary to generate the vaccine recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification in light of the high degree of unpredictability in the art regarding which structural features are required in order to provide protection, the absence of working examples directed to

same, the complex nature of the invention, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 2-14, 16-30 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

> (MPEP 2163) The satisfaction of the enablement requirement does not satisfy the written description requirement. See *In re Barker*, 559 F.2d 588, 591, 194 USPQ 470, 472 (CCPA 1977) (a specification may be sufficient to enable one skilled in the art to make and use the invention, but still fail to comply with the written description requirement). See also *In re DiLeone*, 436 F.2d 1404, 1405, 168 USPQ 592, 593 (CCPA 1971). For the written description requirement, an applicant's specification must reasonably convey to those skilled in the art that the applicant was in possession of the claimed invention as of the date of invention. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997); *Hyatt v. Boone*, 146 F.3d 1348, 1354, 47 USPQ2d 1128, 1132 (Fed. Cir. 1998).

In this instance applicants are claiming a PRE nucleic acid that has at least 80% sequence similarity with SEQ ID NO: 1, the portion of the sequence that is critical has not been sufficiently described in terms of their structure and function. Claiming a product based on function does not provide sufficient description of the product. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological or pharmacological activities. Therefore, structurally unrelated "molecules" encompassed by the claimed invention other than those disclosed in the specification as filed would be expected to have greater differences in their structural and

functional characteristics and attributes. Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required

> "a mere wish or plan" for obtaining an invention is not enough to comply with § ll2, ¶ 1(*Regents of the University of California v. Eli Lilly & Co., 119* F.3d 559, at 1566).
>
> The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

The instant specification and claims do not provide sufficient functional and structural characteristics of PRE coupled with a known or disclosed correlation between function and structure. Since the disclosure fails to describe the common attributes or characteristics that identify members of the group, the disclosure of particular compounds is insufficient to describe the genus of molecules, encompassed by the claimed invention.

In this instance applicants are claiming a PRE nucleic acid that has at least 80% or 90% sequence similarity with SEQ ID NO: 1 and the product has not been sufficiently described in terms of their structure and function. In order to overcome the written description deficiency applicant may: define the structure of the target that is critical for activity of decreasing particle production and is shared by all members of "the family" of nucleic acids which make up the PRE nucleic acid that has at least 80% sequence similarity with SEQ ID NO: 1. Therefore there is lack of written description of for a PRE that has PRE nucleic acid that has at least 90% or 80% sequence similarity with SEQ ID NO: 1.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Gene bank Accession # C80740 or C80177.

The instant invention is drawn to a nucleic acid comprising SEQ ID NO 1, this nucleic acid would have certain properties if inserted into a recombinant virus. The mere recitation of newly-discovered function or property, inherently possessed by things in the prior art, does not cause the claim drawn to those things to distinguish over the prior art (See *In re Best, Bolton, and Shaw* 195 USPQ 430 (CCPA 1977), *In re Schreiber* 44 USPQ2d 1429)

The cited accession numbers disclose SEQ ID NO:1, in order to obtain a nucleic acid sequence using conventional technology, the nucleic acids have to first be purified from the source, in this case a mouse. Therefore the instant invention is anticipated by the nucleic acid sequences disclosed in the GeneBank.

The rejection can be overcome by indicating that the isolated nucleic acid comprising the PRE of SEQ ID NO:1 is part of a NCTE-deficient hybrid virus.

Conclusion

Claims 2-20 and 30 are objected to.

Claims 1-29 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The official fax phone number for the organization where this application or proceeding is assigned is 703-872-9306; for informal communications please use 703-746-3162.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD.
PATENT EXAMINER 10/20/03